09/578,693 WCOOK 12/27/04

## (FILE 'HOME' ENTERED AT 20:50:54 ON 24 DEC 2004)

|    | FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT |
|----|---|
|    | 20:51:16 ON 24 DEC 2004   |
| L1 | 6331 S FABP?  |
| L2 | 2140 S L1 AND LIVER?  |
| L3 | 927 S (L FABP)  |
| L4 | 20 S L3 AND RENAL?  |
| L5 | 38 S L3 AND KIDNEY?   |
| L6 | 12 DUPLICATE REMOVE L4 (8 DUPLICATES REMOVED)                       |
| L7 | 25 DUPLICATE REMOVE L5 (13 DUPLICATES REMOVED)                      |

=>

## (FILE 'HOME' ENTERED AT 20:50:54 ON 24 DEC 2004)

|    | FILE 'BIOSIS, CAPLUS, EMBASE, | MEDLINE, CANCERLIT, JAPIO' ENTERED AT |
|----|-------------------------------|---------------------------------------|
|    | 20:51:16 ON 24 DEC 2004       |                                       |
| L1 | 6331 S FABP?                  |                                       |
| L2 | 2140 S L1 AND LIVER?          |                                       |
| L3 | 927 S (L FABP)                |                                       |
| L4 | 20 S L3 AND RENAL?            |                                       |
| L5 | 38 S L3 AND KIDNEY?           |                                       |
| L6 | 12 DUPLICATE REMOVE I         | 4 (8 DUPLICATES REMOVED)              |
| L7 | 25 DUPLICATE REMOVE I         | 5 (13 DUPLICATES REMOVED)             |

ANSWER 20 OF 25 MEDLINE on STN

93352664 MEDLINE AN

PubMed ID: 8349710 DN

- Use of transgenic mice to map cis-acting elements in the liver fatty TТ acid-binding protein gene (Fabpl) that regulate its cell lineage-specific, differentiation-dependent, and spatial patterns of expression in the gut epithelium and in the liver acinus.
- AU Simon T C; Roth K A; Gordon J I
- Department of Molecular Biology, Washington University School of Medicine, CS St. Louis, Missouri 63110.
- NC DK30292 (NIDDK)
- Journal of biological chemistry, (1993 Aug 25) 268 (24) 18345-58. SO Journal code: 2985121R. ISSN: 0021-9258.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LΑ English
- FS Priority Journals
- EM 199309
- Entered STN: 19931001 ED

Last Updated on STN: 19931001

Entered Medline: 19930916

Axial pattern formation is sustained in the mammalian gut epithelium AB despite rapid and continuous renewal of its four principal cell lineages. The mouse and rat liver fatty acid-binding protein (L-

FABP) genes (Fabpl) represent an excellent model for understanding the mechanisms that determine differentiation-dependent, cell lineage-specific, and distinct regional patterns of expression along the crypt-to-villus and duodenal-to-ileal axes of the gut, as well as within the liver acinus. We have used transgenic mice to map cis-acting elements in rat Fabpl that control these patterns of gene expression. transgenes were analyzed, representing sequential deletions of the 5'-nontranscribed domain of Fabpl linked to the human growth hormone (hGH) gene beginning at its nucleotide +3 (L-FABP/hGH+3).

Several pedigrees of mice containing each one of the L-

FABP/hGH+3 transgenes were examined at the end of their 8th and 20th weeks of postnatal life using immunocytochemical and RNA hybridization analyses. A remarkably compact sequence spanning nucleotides -132 to +21 of Fabpl is sufficient to establish and maintain a distribution of reporter mRNA and protein in villus-associated enterocytes located along the duodenal-to-ileal axis of the gut that resembles the pattern of expression of the endogenous Fabpl gene.

FABP-132 to +21/hGH+3 is also expressed in surface and pit mucous cells of gastric units and in enterocytes located in the colonic homologs of small intestinal villi, the surface epithelial cuffs. This pattern of transgene expression in the stomach and colon recapitulates that of the intact endogenous donor rat Fabpl but not that of mouse Fabpl, which is silent in these proximal and distal segments of the gastrointestinal tract. Analysis of mice containing L-FABP-4000 to

+21/hGH+3, L-FABP-1600 to +21/hGH+3, L-

FABP-596 to +21/hGH+3, L-FABP-246 to

+21/hGH+3, and L-FABP-186 to +21/hGH+3 indicate that

Fabpl's cephalocaudal gradient is influenced by cis-acting suppressors of cecal and colonic expression located between nucleotides -4000 and -1600 and by cis-acting activators of cecal and colonic expression located between nucleotides -597 and -351. L-FABP-132 to

+21/hGH+3 is precociously activated in proliferating and nonproliferating epithelial cells located in intestinal crypts. The suppressor(s) of L-FABP accumulation in crypt epithelial cell populations

are not represented between nucleotides -4000 and +21, indicating that different cis-acting sequences regulate regional and differentiationdependent patterns of Fabpl expression. (ABSTRACT TRUNCATED AT 400 WORDS)

CTAging: ME, metabolism

```
Animals
Base Sequence
*Carrier Proteins: BI, biosynthesis
*Carrier Proteins: GE, genetics
Cell Differentiation
Digestive System: CY, cytology
*Digestive System: ME, metabolism
Epithelial Cells
Epithelium: ME, metabolism
Fatty Acids: ME, metabolism
Growth Hormone: BI, biosynthesis
Growth Hormone: BL, blood
Growth Hormone: GE, genetics
Humans
Immunohistochemistry
In Situ Hybridization
  Kidney: CY, cytology
  Kidney: ME, metabolism
Liver: CY, cytology
*Liver: ME, metabolism
Mice
Mice, Transgenic
Molecular Sequence Data
*Neoplasm Proteins
*Nerve Tissue Proteins
Oligodeoxyribonucleotides
Organ Specificity
RNA, Messenger: IP, isolation & purification
*RNA, Messenger: ME, metabolism
```

Research Support, U.S. Gov't, P.H.S.

```
ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation.
     STN
     1999:516866 BIOSIS
AN
     PREV199900516866
DN
     Urinary excretion of fatty acid binding protein (L-FABP
TΙ
     ) reflects the stress on the proximal tubule and a marker of progression
     of renal damage.
     Kamijo, A. [Reprint author]; Yamanouchi, M.; Sugaya, T.; Nomata, Y.;
ΑU
     Hirano, N.; Hase, H.; Oba, S. [Reprint author]; Suzuki, N. [Reprint
     author]; Miyashita, K. [Reprint author]; Hirata, Y. [Reprint author];
     Goto, A. [Reprint author]; Fujita, T. [Reprint author]; Omata, M. [Reprint
     author]; Kimura, K. [Reprint author]
CS
     Internal Medicine, University of Tokyo, Tokyo, Japan
     Journal of the American Society of Nephrology, (Sept., 1999) Vol. 10, No.
SO
     PROGRAM AND ABSTR. ISSUE, pp. 106A. print.
    Meeting Info.: 32nd Annual Meeting of the American Society of Nephrology.
    Miami Beach, Florida, USA. November 1-8, 1999. American Society of
     Nephrology.
     CODEN: JASNEU. ISSN: 1046-6673.
     Conference; (Meeting)
DT
     Conference; Abstract; (Meeting Abstract)
T.A
     English
     Entered STN: 3 Dec 1999
ED
     Last Updated on STN: 3 Dec 1999
CC
     Urinary system - Pathology
                                  15506
     Physiology - Stress
                           12008
    Metabolism - Lipids
                           13006
    Metabolism - Proteins, peptides and amino acids
     General biology - Symposia, transactions and proceedings
                                                                 00520
     Urinary system - Physiology and biochemistry
     Urinary system - Anatomy
                                15502
     Biochemistry studies - Proteins, peptides and amino acids
                                                                  10064
     Biochemistry studies - Lipids
                                     10066
    Major Concepts
IT
        Nephrology (Human Medicine, Medical Sciences)
ΙT
     Chemicals & Biochemicals
        L-fatty acid binding protein: proximal tubule stress reflection,
        renal damage progression marker, urinary excretion
IT
    Miscellaneous Descriptors
        Meeting Abstract
ORGN Classifier
        Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
```

```
ANSWER 9 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
    1999:359733 CAPLUS
AΝ
DN
    130:349390
    Entered STN: 11 Jun 1999
ED
    Method for examining kidney diseases.
TI
    Yamanouchi, Masaya; Honda, Akiko; Uchida, Hiromi; Sugaya, Takeshi; Kimura,
IN
    Tanabe Seiyaku Co., Ltd., Japan
PA
SO
    PCT Int. Appl., 31 pp.
    CODEN: PIXXD2
DT
    Patent
    Japanese
LΑ
    ICM G01N033-53
IC
    9-10 (Biochemical Methods)
CC
    Section cross-reference(s): 14, 15
                              DATE APPLICATION NO. DATE
    PATENT NO.
                      KIND
                       ____
                                       WO 1998-JP5319
                       A1 19990603
                                                              19981126
PΤ
    WO 9927363
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, KE, KG,
            KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
            NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
            UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                       TW 1998-87119150
    TW 562926
                        В
                              20031121
                        A2
                              19990907
                                        JP 1998-331828
                                                               19981124
    JP 11242026
                              20020225
    JP 3259768
                       В2
    AU 9912603
                       A1
                              19990615
                                        AU 1999-12603
                                                               19981126
                                        EP 1998-955936
                       A1
    EP 1043587
                           20030604
                              20001011
                                                               19981126
                       В1
    EP 1043587
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
                              20030615
                                        AT 1998-955936
    AT 242484
                                                               19981126
                        \mathbf{E}
PRAI JP 1997-323684
                              19971126
                      Α
    WO 1998-JP5319
                       W
                              19981126
CLASS
              CLASS PATENT FAMILY CLASSIFICATION CODES
WO 9927363
              ICM
                      G01N033-53
WO 9927363
              ECLA
                      G01N033/68V
EP 1043587
            ECLA G01N033/68V
    A diagnostic method is described for examining kidney diseases by immunol.
    detecting a fatty acid-binding protein derived from ki
```

AB

ANSWER 18 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN 89265049 EMBASE AN DN 1989265049 Mechanism of hepatic fatty acid uptake. ΤI Stremmel W. ΑU Abteilung fur Gastroenterologie des Zentrums fur Innere Medizin der CS Universitatskliniken Dusseldorf, 4000 Dusseldorf, Germany Journal of Hepatology, (1989) 9/3 (374-382). SO ISSN: 0168-8278 CODEN: JOHEEC CY Netherlands Journal DT029 Clinical Biochemistry FS 048 Gastroenterology LΑ English SL English AΒ In recent years a new concept of the mechanism of hepatic fatty acid uptake has been described. It was shown that this major class of energy yielding substraters enters hepatocytes by a carrier-mediated uptake system. After the dissociation of the fatty acid-albumin complex at the sinusoidal liver cell plasma membrane, fatty acid binds with high affinity to a specific, newly identified, 40 kDa membrane fatty acid binding protein (MFABP). This protein functions as transmembrane transporter for long chain fatty acids. Hepatocellular uptake of fatty acids was shown to be sodium-dependent and electrogenic, compatible with a Na+-fatty acid cotransport system. Medical Descriptors: CT\*cell membrane \*electrochemical gradient \*liver function

\*membrane transport

review

human

priority journal

Drug Descriptors:

\*fatty acid

ANSWER 18 OF 20 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 89265049 EMBASE

DN 1989265049

TI Mechanism of hepatic fatty acid uptake.

AU Stremmel W.

CS Abteilung fur Gastroenterologie des Zentrums fur Innere Medizin der Universitatskliniken Dusseldorf, 4000 Dusseldorf, Germany

SO Journal of Hepatology, (1989) 9/3 (374-382). ISSN: 0168-8278 CODEN: JOHEEC

CY Netherlands

DT Journal

FS 029 Clinical Biochemistry 048 Gastroenterology

LA English

SL English

AB In recent years a new concept of the mechanism of hepatic fatty acid uptake has been described. It was shown that this major class of energy yielding substraters enters hepatocytes by a carrier-mediated uptake system. After the dissociation of the fatty acid-albumin complex at the sinusoidal liver cell plasma membrane, fatty acid binds with high affinity to a specific, newly identified, 40 kDa membrane fatty acid binding protein (MFABP).

This protein functions as transmembrane transporter for long chain fatty acids. Hepatocellular uptake of fatty acids was shown to be sodium-dependent and electrogenic, compatible with a Na+-fatty acid cotransport system.

CT Medical Descriptors:

\*cell membrane

\*electrochemical gradient

\*liver function

\*membrane transport

review

human

priority journal
Drug Descriptors:

\*fatty acid

```
ANSWER 15 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
     1993:188195 CAPLUS
AN
DN
     118:188195
     Entered STN: 14 May 1993
ED
     Liver plasma membrane fatty acid
TI
     binding protein
ΑU
     Potter, Barry J.; Berk, Paul D.
     Dep. Med., Mount Sinai Sch. Med., New York, NY, 10029, USA
CS
     Hepatic Transp. Bile Secretion (1993), 253-67. Editor(s): Tavoloni,
SO
     Nicola; Berk, Paul D. Publisher: Raven, New York, N. Y.
     CODEN: 58QLAU
     Conference; General Review
DT
     English
LA
     13-0 (Mammalian Biochemistry)
CC
AΒ
     A review, with 56 refs., on: cell surface events and the albumin
     receptor hypothesis; isolation of the plasma membrane
     fatty acid-binding protein;
     characterization of the fatty acid-binding
     protein; and if the plasma membrane fatty
     acid binding protein related to mitochondrial
     glutamic-oxalacetic transaminase.
ST
     review liver fatty acid
     binding protein
     Liver, composition
        (fatty acid-binding proteins of
        membrane of)
     Cell membrane
IT
        (fatty acid-binding proteins
        of, of liver)
IT
     Proteins, specific or class
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (FABP (fatty acid-binding protein
```

), of liver cell membrane)

```
ANSWER 15 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
     1993:188195 CAPLUS
AN
     118:188195
DN
     Entered STN: 14 May 1993
ED
ΤI
     Liver plasma membrane fatty acid
     binding protein
     Potter, Barry J.; Berk, Paul D.
ΑU
     Dep. Med., Mount Sinai Sch. Med., New York, NY, 10029, USA
CS
     Hepatic Transp. Bile Secretion (1993), 253-67. Editor(s): Tavoloni,
SO
     Nicola; Berk, Paul D. Publisher: Raven, New York, N. Y.
     CODEN: 58QLAU
DT
     Conference; General Review
     English
LΑ
     13-0 (Mammalian Biochemistry)
CC
AB
     A review, with 56 refs., on: cell surface events and the albumin
     receptor hypothesis; isolation of the plasma membrane
     fatty acid-binding protein;
     characterization of the fatty acid-binding
     protein; and if the plasma membrane fatty
     acid binding protein related to mitochondrial
     glutamic-oxalacetic transaminase.
ST
     review liver fatty acid
     binding protein
ΙT
     Liver, composition
        (fatty acid-binding proteins of
        membrane of)
IT
     Cell membrane
        (fatty acid-binding proteins
        of, of liver)
     Proteins, specific or class
IT
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (FABP (fatty acid-binding protein
```

), of liver cell membrane)

ANSWER 12 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN 1997:88191 CAPLUS AN DN 126:167969 Entered STN: 06 Feb 1997 ED Fatty acid-binding proteins. Their TТ structure, function and gene expression ΑU Fujii, Hiroshi Sch. Med., Niigata Univ., Niigata, Japan CS Domyaku Koka (1996), 24(7/8), 353-361 so CODEN: DOMKDM; ISSN: 0386-2682 PBNippon Domyaku Koka Gakkai DTJournal; General Review LΑ Japanese CC 6-0 (General Biochemistry) A review with 45 refs., on the mol. structures, genes, and biol. AB functions of fatty acid-binding protein (FABP). Lipid-binding, -transfer or -exchange proteins are present in intra- and extracellular fluids of all organisms. They play a role in the transport or targeting of lipids in the cell or in the plasma, but may also interact directly or indirectly by modulation of various cellular processes. The structure of these families of lipid-binding proteins, albumin, lipocalin and fatty acid-binding protein (FABP) families, has been established. FABP have similar mol. masses (14-15 kDa) and amino acid compns., exhibit some sequences similarity (38-70%), and form a family with other hydrophobic ligand-binding proteins such as cellular retinol-binding protein (CRBP), cellular retinoic acid-binding protein (CRABP) and intestinal bile acid-binding protein (I-BABP/I-15P/ILBP). At least, 7 types of FABP, liver (L), intestine (I), heart (H), brain (B), myelin (mP2), adipocyte (aP2) or skin type (E/C) FABP, have been isolated from various sources. The large similarity of H-HABP, aP2, mP2, and E/C-FABP (60-70%) is reflected in the similar amino acids on essential positions for fatty acid binding. Interestingly, these FABPs and CRBP I and II contain a protein tyrosine kinase recognition sequence before Tyr 19. The physiol. relevance of tyrosine phosphorylation of FABP remains unclear. Furthermore, recently, a significant degree of primary sequence similarity was noted between a domain of an ion channel, the N-methyl-D-aspartate receptor and the members of the FABP family, while the significance of FABP-like domain for ion channel regulation remains unknown. X-ray diffraction anal. of FABP family proteins revealed that the show a structure of 2 short  $\alpha$ -helixes located near N terminus and followed by 10 anti-parallel  $\beta$ -strands. The  $\beta$ -strands are organized into 2 nearly orthogonal  $\beta\text{--sheets}$  giving the protein the overall appearance of a "clam shell". To date, the genes for 9 members of the FABP family have been identified. The overall organization of the genes is identical, 4 exons and 3 introns. The exon/intron boundaries are similar in all genes but the length of the intron sequences varies markedly. Although FABP has been thought to be involved in the intracellular transport and metabolism of long-chain fatty acids or other hydrophobic ligands, their physiol. roles in cells are not precisely understood. Intracellular fatty acids are important mols. for energy delivery and for synthesis of membrane lipid mediators such as eicosanoids. Apart from their functioning as metabolic substrates and constituents of complex lipids, long-chain fatty acids are being recognized as elements of several cell-to-cell signal transduction pathways. Therefore, it would be interesting to examine mechanisms of the action of FABP involved in these cellular signal transduction. review FABP protein structure gene function ST Proteins, specific or class RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study); PROC (Process)

ANSWER 12 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN 1997:88191 CAPLUS AN DN 126:167969 Entered STN: 06 Feb 1997 ED TI Fatty acid-binding proteins. Their structure, function and gene expression ΑU Fujii, Hiroshi CS Sch. Med., Niigata Univ., Niigata, Japan Domyaku Koka (1996), 24(7/8), 353-361 SO CODEN: DOMKDM; ISSN: 0386-2682 PB Nippon Domyaku Koka Gakkai DT Journal; General Review LA Japanese CC 6-0 (General Biochemistry) A review with 45 refs., on the mol. structures, genes, and biol. AΒ functions of fatty acid-binding protein (FABP). Lipid-binding, -transfer or -exchange proteins are present in intra- and extracellular fluids of all organisms. They play a role in the transport or targeting of lipids in the cell or in the plasma, but may also interact directly or indirectly by modulation of various cellular processes. The structure of these families of lipid-binding proteins, albumin, lipocalin and fatty acid-binding protein (FABP) families, has been established. FABP have similar mol. masses (14-15 kDa) and amino acid compns., exhibit some sequences similarity (38-70%), and form a family with other hydrophobic ligand-binding proteins such as cellular retinol-binding protein (CRBP), cellular retinoic acid-binding protein (CRABP) and intestinal bile acid-binding protein (I-BABP/I-15P/ILBP). At least, 7 types of FABP, liver (L), intestine (I), heart (H), brain (B), myelin (mP2), adipocyte (aP2) or skin type (E/C) FABP, have been isolated from various sources. The large similarity of H-HABP, aP2, mP2, and E/C-FABP (60-70%) is reflected in the similar amino acids on essential positions for fatty acid binding. Interestingly, these FABPs and CRBP I and II contain a protein tyrosine kinase recognition sequence before Tyr 19. The physiol. relevance of tyrosine phosphorylation of FABP remains unclear. Furthermore, recently, a significant degree of primary sequence similarity was noted between a domain of an ion channel, the N-methyl-D-aspartate receptor and the members of the FABP family, while the significance of FABP-like domain for ion channel regulation remains unknown. X-ray diffraction anal. of FABP family proteins revealed that the show a structure of 2 short  $\alpha$ -helixes located near N terminus and followed by 10 anti-parallel  $\beta$ -strands. The  $\beta$ -strands are organized into 2 nearly orthogonal  $\beta\mbox{-sheets}$  giving the protein the overall appearance of a "clam shell". To date, the genes for 9 members of the FABP family have been identified. The overall organization of the genes is identical, 4 exons and 3 introns. The exon/intron boundaries are similar in all genes but the length of the intron sequences varies markedly. Although FABP has been thought to be involved in the intracellular transport and metabolism of long-chain fatty acids or other hydrophobic ligands, their physiol. roles in cells are not precisely understood. Intracellular fatty acids are important mols. for energy delivery and for synthesis of membrane lipid mediators such as eicosanoids. Apart from their functioning as metabolic substrates and constituents of complex lipids, long-chain fatty acids are being recognized as elements of several cell-to-cell signal transduction pathways. Therefore, it would be interesting to examine mechanisms of the action of FABP involved in these cellular signal transduction. STreview FABP protein structure gene function Proteins, specific or class RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL

(Biological study); PROC (Process)

```
(FABP (fatty acid-binding protein
    ); mol. structure, function, and gene expression of fatty
        acid-binding proteins)

IT Gene, animal
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
    (Biological study); PROC (Process)
        (mol. structure, function, and gene expression of fatty
        acid-binding proteins)
```

```
(FABP (fatty acid-binding protein
    ); mol. structure, function, and gene expression of fatty
        acid-binding proteins)

IT Gene, animal
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
    (Biological study); PROC (Process)
        (mol. structure, function, and gene expression of fatty
        acid-binding proteins)
```